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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/607,623	06/27/2003	Haim D. Danenberg	4313-4005	7907

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EXAMINER	
JAGOE, DONNA A	
ART UNIT	**PAPER NUMBER**
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/607,623	DANENBERG ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41 and 64-69* is/are pending in the application.

4a) Of the above claim(s) *2,3,10-15,18,21,22,27-30 and 66-69* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-9,16,17,19,20,23-26,31-41,64 and 65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/28/05 and 2/2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of claims 1-41 in the reply filed on July 26, 2006 is acknowledged. The traversal is on the ground(s) that Groups I and III be examined together. Applicant states that Group I is directed to a method of treating acute myocardial infarction. Group III is directed to a method of reducing the zone of infarct using bisphosphonate. Group III is a narrower invention of the Group I invention and as such is encompassed by Group I. There is no additional burden on the Examiner in searching prior art in an area encompassed by the elected group. This is further evidenced by the fact that both Group I and Group III are classified in class 514, as set forth by the Restriction. This is found to be persuasive, however in view of the election of species of (A) and encapsulated agent (B) an intracellular inhibitor and (C) a bisphosphonate, claims 2, 3, 10-15, 18, 21, 22, 27-30, and 66-69 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on July 26, 2006.

Accordingly, claims 1, 4-9, 16, 17, 19, 20, 23-26, 31-41, 64 and 65 are presented for examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38, 40 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "a method of treating a patient with an acute myocardial infarction" (AMI) in line 1 of the claim. Claims 38, 40 and 41 are drawn to the method of treating a patient wherein the myocardial infarction is anticipated or probable, however these claims depend from any one of claims 1-3, 25, 27 or 29 wherein the myocardial infarction has occurred. There is insufficient antecedent basis for these limitations in the claims. Correction is necessary.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6-9, 20 rejected under 35 U.S.C. 103(a) as being unpatentable over Hope et al. U.S. Patent No. 6,139,871 A.

Hope et al. teach encapsulated agents such as liposomes with an average diameter of 100 - 150 nanometers (0.1 - 0.15 microns) for treatment of atherosclerosis (see abstract). It does not teach the liposomes to treat a patient with an acute myocardial infarction. However, Hope et al. teach that atherosclerosis in the vessel walls can occlude the vessel lumen and obstruct blood flow through the vessel causing ischemia. The most common form of ischemic end organ damage is myocardial infarction and cerebrovascular accidents (column 1, lines 17-24). It would have been made obvious to one of ordinary skill in art at the time it was made to infuse encapsulated agents such as liposomes in a size of 0.1 to 0.15 microns to treat atherosclerosis motivated by the teaching of Hope et al. that atherosclerosis leads to occlusion and end organ damage such as myocardial infarction.

Claims 1, 4-9, 16, 17, 19, 20, 23-26, 31-38, 40, 41, 64 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ylitalo, Gen. Pharmacol. 2002 in view of Hope et al. U.S. Patent No. 6,139,871 A.

Ylitalo teaches liposomal (encapsulated) formulations of bisphosphonates such as clodronate and etidronate (page 293, column 2, paragraph 3), and teach that bisphosphonates inhibit atherosclerosis (page 287, column 1 to page 288, column 2). Ylitalo teaches that bisphosphonates the anti-atherogenic effect is due to a direct effect on arterial wall wherein the bisphosphonates interact with the subendothelial lipid phagocyting cells (page 292, column 1, paragraph 1) and macrophages are especially sensitive to bisphosphonates, and bisphosphonates suppress macrophages and exert cytotoxicity and suppress the appearance of macrophages in arterial wall during atherogenesis. Ylitalo does not teach depletion of macrophages, however, it teaches that the appearance of macrophages is suppressed. Since the term "depletion" is synonymous with the term "eliminating all macrophages", and both circumscribe methods of treatment having absolute success. Absolute success is not reasonably possible with most diseases, especially ones having etiologies as complex as atherosclerosis and AMI. Ylitalo does not teach treatment of a patient with AMI or reducing the zone of infarct following an AMI and it does not teach the size of the liposomes. However, Hope et al. teach that atherosclerosis in the vessel walls can occlude the vessel lumen and obstruct blood flow through the vessel causing ischemia. The most common form of ischemic end organ damage is myocardial infarction and cerebrovascular accident (column 1, lines 17-24). Hope et al. teach liposomes of 0.1 to

0.15 microns. It would have been made obvious to one of ordinary skill in art at the time it was made to treat AMI in a patient by administering encapsulated bisphosphonates in liposomes in a size of 0.1 to 1 micron motivated by the teaching of Ylitalo who teaches liposomal (encapsulated) formulations of bisphosphonates such as clodronate and etidronate (page 293, column 2, paragraph 3), and that bisphosphonates inhibit atherosclerosis and the teaching of Hope et al. that atherosclerosis leads to occlusion and end organ damage such as myocardial infarction.

Claims 1, 4-9, 16, 17, 19, 20, 23-26, 31-41, 64 and 65 are rejected under 35 U.S.C. 103(a) as being obvious over Golomb et al. U.S. Patent No. 6,719,998 B1. in view of Hope et al. U.S. Patent No. 6,139,871 A.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer

in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2). Golumb et al. teach treatment of restenosis (claim 1) and coronary restenosis (claim 5), by administering a liposomal bisphosphonate of 0.1 to 1.0 microns. One cannot treat restenosis unless stenosis or post angioplasty narrowing has occurred. Hope et al. teach that atherosclerosis in the vessel walls can occlude the vessel lumen and obstruct blood flow through the vessel causing ischemia. The most common form of ischemic end organ damage is myocardial infarction and cerebrovascular accident (column 1, lines 17-24). It would have been made obvious to one of ordinary skill in art at the time it was made to treat AMI and reduce the zone of infarction by employing encapsulated agents such as liposomal bisphosphonates motivated by the teaching of Golumb et al. who teaches treatment of restenosis (claim 1) and coronary restenosis (claim 5), by administering a liposomal bisphosphonate of 0.1 to 1.0 microns and Hope et al. that atherosclerosis leads to occlusion and end organ damage such as myocardial infarction.

Claims 1, 4-9, 16, 17, 19, 20, 23-26, 31-41, 64 and 65 are rejected under 35 U.S.C. 103(a) as being obvious over Golomb et al. U.S. Patent No. 6,984,400 B2. and Hope et al. U.S. Patent No. 6,139,871 A.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome

by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2). Golomb et al teach treating restenosis by administering a bisphosphonate in *inter alia* liposomes in sizes of from 0.01 to 1.0 microns (see claim 1). It teaches phagocytosis of bisphosphonate particles by inhibiting macrophages/monocytes (column 2, lines 23-65). It does not teach AMI. One cannot treat restenosis unless stenosis or post angioplasty narrowing has occurred. Hope et al. teach that atherosclerosis in the vessel walls can occlude the vessel lumen and obstruct blood flow through the vessel causing ischemia. The most common form of ischemic end organ damage is myocardial infarction and cerebrovascular accident (column 1, lines 17-24). It would have been made obvious to one of ordinary skill in art at the time it was made to treat AMI with encapsulated agents such as liposomal bisphosphonates motivated by the teaching of Golumb et al. who teaches treatment of restenosis (claim 1) by administering a liposomal bisphosphonate

of 0.1 to 1.0 microns and Hope et al. that atherosclerosis leads to occlusion and end organ damage such as myocardial infarction.

Claims 1, 4-9, 16, 17, 19, 20, 23-26, 31-41, 64 and 65 are rejected under 35 U.S.C. 103(a) as being obvious over Golomb et al. U.S. Patent No. 7,008,645 B2.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2). Golomb et al teach treating restenosis by administering encapsulated bisphosphonate) see abstract) such as liposomes (column 5, lines 43-44) in sizes of from 0.01 to 1 micron (column 9, lines 55-58). It teaches that bisphosphonates inactivate monocytes/macrophages (column 5, lines 4-7). It does not teach AMI. One cannot treat restenosis unless stenosis or

post angioplasty narrowing has occurred. Hope et al. teach that atherosclerosis in the vessel walls can occlude the vessel lumen and obstruct blood flow through the vessel causing ischemia. The most common form of ischemic end organ damage is myocardial infarction and cerebrovascular accident (column 1, lines 17-24). It would have been made obvious to one of ordinary skill in art at the time it was made to treat AMI with encapsulated agents such as liposomal bisphosphonates motivated by the teaching of Golumb et al. who teaches treatment of restenosis (abstract) by administering a liposomal bisphosphonate and Hope et al. that atherosclerosis leads to occlusion and end organ damage such as myocardial infarction.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Thursday from 9:00 A.M. - 3:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe
Patent Examiner
Art Unit 1614

February 5, 2007

Ardin H. Marschel 2/5/07
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SUPERVISORY PATENT EXAMINER